Quantitative Measure of Stability in Gene Regulatory Networks

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Abstract

A quantitative measure of stability in stochastic dynamics starts to emerge in recent experiments on bioswitches. This quantity, similar to the potential function in mathematics, is deeply rooted in biology, dated back at the beginning of quantitative description of biological processes: the adaptive landscape of Wright (1932) and the development landscape of Waddington (1940). Nevertheless, its quantitative implication has been frequently challenged by biologists. Recent progresses in quantitative biology begin to meet those outstanding challenges.

With the successful experimental work and theoretical analysis on simple artificial gene networks [1], Acar et al [2] further explored the quantitative behaviors in a living gene regulatory network, the yeast galactose-signaling network. Their work provides a fine and new example of quantitative understanding of the stability and reversibility of cellular differentiation state in terms of the potential or energy landscape. I wish to point out here that together with the extensive, and perhaps more quantitative, study in another living genetic regulatory network not discussed by Acar et al, the phage lambda [3,4,5], where similar conclusion was obtained [6], a powerful theoretical modelling framework of stochastic dynamics in biological networks begins to emerge.

There has been a long tradition in biology to understand the stability problem in terms of potential landscape also not mentioned by Acar et al. In 1932 S. Wright proposed the adaptive landscape in evolution in the context of genetics [7]. In 1940 C.H. Waddington proposed the developmental landscape to understand the stability and differentiation in developmental biology [8]. In the context directly linked to bio-switching phenomena M. Delbruck proposed in 1949 that the potential landscape could be used for the modelling [9]. Unfortunately, despite such a continuous effort in biology and the fact that such a landscape concept have been permeated into other fields such as physics and engineering, the potential landscape has been at best viewed in biology as a useful metaphor. It has been generally believed that this concept could not be quantified [10]. It should be instructive to mention that in the general setting of nonequilibrium processes, stochastic dynamical processes in life sciences as discussed in [2] and [6] are obviously belong to this category, the search for such a quantitative potential landscape has been performed during past a few decades and has only been partially successful [11]. Such a difficulty may also be reflected in the debate in mathematics around the catastrophe theory, such as vector vs gradient fields [12].

Those recent studies [1,2,6] reveal that a potential landscape concept is not only metaphoric, also quantitative. An attempt to put in this concept into a rigorous mathematical framework has been under way [13], though various obstacles still lie ahead. It appears that the time is ripe to consider the theoretical modelling from another perspective deeply rooted in biology.

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